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Helicobacter pylori Isolated from the Domestic Cat: Public Health Implications

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***Helicobacter pylori* has been directly linked with active chronic gastritis, peptic ulceration, and gastric adenocarcinoma in humans. Although a substantial portion of the human population is colonized with *H. pylori*, the patterns of transmission of the organism remain in doubt, and reservoir hosts have not been identified. This study documents the isolation of *H. pylori* from domestic cats obtained from a commercial vendor. The isolation of *H. pylori* from these cats was confirmed by morphologic and biochemical evaluations, fatty acid analysis, and 16S rRNA sequence analysis. *H. pylori* was cultured from 6 cats and organisms compatible in appearance with *H. pylori* were observed in 15 additional cats by histologic examination. In most animals, *H. pylori* was present in close proximity to mucosal epithelial cells or in mucus layers of the glandular or surface epithelium. Microscopically, *H. pylori*-infected cat stomachs contained a mild to severe diffuse lymphoplasmacytic infiltrate with small numbers of neutrophils and eosinophils in the subglandular and gastric mucosae. Lymphoid follicles were also noted, particularly in the antrum, and often displaced glandular mucosal tissue. Thus, the domestic cat may be a potential model for *H. pylori* disease in humans. Also, the isolation of *H. pylori* from domestic cats raises the possibility that the organism may be a zoonotic pathogen, with transmission occurring from cats to humans.**

Although spiral organisms were first observed in the gastric mucosa of cats and dogs over 90 years ago, their presence has largely been ignored (1). However, since the discovery of *Helicobacter pylori* in 1983, and its identification as the causative agent of active chronic gastritis and duodenal ulcer disease and as a probable cofactor in the formation of gastric adenocarcinoma in humans, interest in the study of gastric spiral bacteria in domestic and laboratory animals has increased (7, 9–11, 13, 14, 24, 32).

Gastric spiral organisms which are larger and have more helical turns than *H. pylori* have been observed in a small number of humans with gastritis and are also commonly observed in both cats and dogs (15, 16, 23, 27, 29). It is suspected that zoonotic infections with spiral organisms other than *H. pylori* occur (23, 27). The large gastric spiral organisms in humans have been given the name "*Gastrospirillum hominis*" (29). Although these organisms are currently uncultivable, a recent analysis based upon 16S rRNA sequencing indicated that organisms with "*G. hominis*" morphology represent at least two new *Helicobacter* species and that a "*Gastrospirillum*" sp. found in lemurs represents a third new *Helicobacter* species (37). All gastric spiral organisms identified to date have been found to be members of the genus *Helicobacter* on the basis of 16S rRNA sequence analysis. It is likely that several additional *Helicobacter* species with "*Gastrospirillum*" morphology will be found in other mammalian species, and some of these will have zoonotic potential.

Cats are known to harbor a variety of gastric spiral organisms (27–31). Gastric spiral organisms were found by histologic examination in over 97% of random-source cats studied in one report (31). A large cultivable gastric spiral bacterium with periplasmic fibers, *Helicobacter felis*, has been fully characterized (27, 34). Gastric spiral organisms without periplasmic fibers and morphologically similar to those seen in humans are also commonly observed in cats (27). The goal of this study was to identify by histologic, culture, and molecular techniques the types of gastric spiral organisms present in different populations of cats from several commercial vendors. From one group of cats, we cultured an organism which we identified as *H. pylori*. Thus, this report describes the first isolation of *H. pylori* from a domesticated species and raises the possibility that cats may be a zoonotic source of *H. pylori* infections in humans.

MATERIALS AND METHODS

Animals. Gastric tissue was collected at necropsy from 29 young adult cats from four different commercial vendors (A, B, C, and D) of research animals. Four, 1, 3, and 21 cats were obtained from vendors A, B, C, and D, respectively. Vendors A, B, and D maintain purpose-bred closed colonies of cats; new animals are introduced infrequently into the existing population. Vendor C cats are from a random-source colony into which new cats are commonly introduced. Approximately equal numbers of males and females composed the study group.

Gastric tissue was harvested from cats used in terminal procedures as part of various research projects. Nine vendor D

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cats and one vendor C cat were used for acute studies of the respiratory tract. These cats were present in the animal research facility for 3 to 10 days. All 4 vendor A cats, the vendor B cat, 2 vendor C cats, and 12 vendor D cats were used in chronic neurologic studies. The length of stay of these cats varied from 3 to 7 months.

After arrival at our research facility, all cats were individually housed for the duration of their stay. Cats were never in direct contact with each other. Water was provided ad libitum in bowls, and the animals were fed laboratory feline diet 5003 (PMI Feeds, Inc., St. Louis, Mo.). None of the animals had clinical signs related to upper gastrointestinal tract disease. No oral medications were administered, nor were gastric intubation, gastroscopy, or any other procedures involving the digestive tract performed on any of the cats.

Impression smears. Small pieces of gastric mucosa from the body and antrum of the stomach were imprinted on glass slides, and the slides were then Gram stained. This procedure was performed for 2 of 4 vendor A animals, 2 of 3 vendor C animals, and 15 of 21 vendor D animals.

Rapid urease testing. Mucosal sections from the body and antral regions of the stomach were placed into tubes containing urea agar (selective rapid urea; Remel, Lenexa, Kans.). The tubes were incubated at room temperature, monitored hourly for 8 h, and evaluated a final time at 24 h. A pink color developing in the gel was considered a positive test. Rapid urease testing was performed for 2 of 3 vendor C animals and 16 of 21 vendor D animals.

Isolation of gastric organisms. Four or five mucosal samples approximately 3 by 3 mm from both the body and the antrum of the stomach were collected for bacterial culturing from one vendor C animal and eight vendor D animals. Culturing for cats from vendors A and B was not attempted. Individual samples were placed in sterile brucella broth (Remel) for transport, ground in a sterile grinder, and then inoculated onto the culture medium. A brucella agar base supplemented with 5% sheep blood and containing trimethoprim, vancomycin, and polymyxin B (brucella TVP agar; Remel) and a chocolate agar base (Remel) were used for initial isolation. All culture plates were incubated for 3 to 5 days at 35 to 37°C in a moist microaerophilic atmosphere provided by either an anaerobic jar with a Campypak system (Campypak Plus; BBL Microbiology Systems, Cockeysville, Md.) or a sealed pouch (Bio-Bag environmental chamber type Cfj; BBL). Cultured organisms were Gram stained to ascertain their staining characteristics and morphology.

Characterization of strains. The following biochemical tests were performed on cultured organisms by standard methods: presence or absence of catalase, oxidase, urease, and alkaline phosphatase; nitrate reduction; H_2S production on triple sugar iron agar; hippurate and indoxyl acetate hydrolysis; sensitivity to cephalothin and nalidixic acid; growth on 3% NaCl; microaerophilic growth at 25 and 42°C; and aerobic growth at 37°C.

Fatty acid analysis. An evaluation of the fatty acid content of strain D01 was performed by use of gas chromatography at an independent laboratory (Microbial ID Inc., Newark, Del.). The results of this analysis were then compared with standard fatty acid profiles of cataloged strains of bacteria by use of the similarity indexes in the Microbial ID Inc. Microbial Identification System (38).

Electron microscopy. Bacteria were negatively stained with 1% phosphotungstic acid (pH 6.5) for 20 to 30 s. Bacteria were then examined with a JEOL JEM-1200 EX transmission electron microscope operating at 100 kV.

Histologic evaluation. The stomach from each cat was opened along the lesser curvature, and the entire organ was placed in 10% buffered formalin. Full-thickness sections of the gastric tissue approximately 1.5 cm in length from the cardia and fundus, body, and pyloric antrum of each cat were embedded in paraffin, cut 5.0 μm thick, and stained with hematoxylin and eosin and with Warthin-Starry silver stain.

Warthin-Starry silver-stained sections were evaluated, on a blindly coded basis, for the presence of organisms and their morphology. The quantity of organisms seen in each 1.5-cm stained tissue section was graded on the following scale: 0, no organisms seen; 1, a few organisms seen (<10 organisms per section); 2, moderate numbers of organisms seen (10 to 50 organisms per section); and 3, large numbers of organisms seen (>50 organisms per section, usually too numerous to count). Hematoxylin- and eosin-stained slides, also read on a blindly coded basis, were evaluated for histopathologic abnormalities. A gastritis score was assigned to each section as follows: 0, normal, 0 to 10 lymphocytes or plasma cells per ×400 field, with no lymphoid aggregates and a normal gastric epithelium; 1, mild gastritis, 10 to 50 lymphocytes or plasma cells per ×400 field, with less than two follicles per ×20 field and a normal epithelium; 2, moderate gastritis, 10 to 50 or more lymphocytes or plasma cells per ×400 field, with two or more follicles per ×20 field; and 3, severe gastritis, 10 to 50 or more lymphocytes or plasma cells per ×400 field and marked epithelial changes. The number of lymphoid follicles present per ×20 field was also noted. The histopathologic results for the vendor B and C cats were not thoroughly analyzed because of the small sample size. The histopathologic findings for cats infected with *H. pylori* (vendor D) were compared with those for cats free of gastric helicobacter-like organisms (vendor A) and therefore used as controls. The average gastritis scores and number of lymphoid follicles present for cats from vendors A and D were

TABLE 1. Oligonucleotide primers used for amplification and sequencing of 16S rRNA

Primer	Type[a]	Sequence (5′ → 3′)[b]	Position[c]	Orientation
1	PCR	AGAGTTTGATYCTGGCT	8–24	Forward
2	PCR	TACGGYTACCTTGTTACGACT	1493–1513	Reverse
3	Seq	ACTGCTGCCTCCCGT	344–358	Reverse
4	Seq	GTRTTACCGCGGCTGCTG	519–536	Reverse
5	Seq	CTACCAGGGTATCTAATC	786–804	Reverse
6	Seq	GGTTGCGCTCGTTGCGGG	1096–1113	Reverse
7	Seq	GGAATCGCTAGTAATCG	1337–1353	Forward
8	Seq	CCCGGGAACGTATTCACCG	1369–1387	Reverse

[a] PCR, primer used for PCR; Seq, primer used for sequencing.
[b] Base codes are standard International Union of Biochemistry codes for bases and ambiguity.
[c] *Escherichia coli* nucleotide numbering.

TABLE 2. Detection of spiral organisms in feline gastric mucosa

Vendor	No. of cats positive/no. tested by:			
	Impression smears[a]	Rapid urease tests	Histologic examinations	Culturing
A	0/2	NA[b]	0/4	NA
B	NA	NA	1/1 (large spirals)[c]	NA
C	2/2 (large spirals)[c]	2/2	3/3 (large spirals)[c]	0/1
D	13/15 (short curved rods)[d]	15/16	22/22 (short curved rods)[d]	6/8 (gram-negative short curved rods)[d]

[a] Gram stained.
[b] NA, not attempted.
[c] Compatible morphologically with *H. felis* or cat "*Gastrospirillum*" sp.
[d] Biochemical or morphologic characteristics compatible with those of *H. pylori*.

compared by use of Student's *t* test. Results were considered statistically significant if P was <0.05.

Crude DNA isolation. Bacteria were cultured on Trypticase soy agar (TSA; Adams Scientific) with 5% sheep blood. A loopfull of cells was harvested, suspended in 100 μl of lysis buffer (50 mM Tris-HCl [pH 7.6], 1 mM EDTA, 0.5% Tween 20, 200 μg of proteinase K per ml), and incubated at 55°C for 2 h. Proteinase K was inactivated by heating to 95°C for 10 min.

Amplification of 16S rRNA cistrons. 16S rRNA cistrons were amplified with primers 1 and 2 (Table 1). PCRs were performed with thin-walled tubes and a Perkin-Elmer 480 thermal cycler. Ten microliters of crude DNA and 1 μM each primer were added to the reaction mixture (final volume, 82 μl). Ampliwax PCR Gem100 (Perkin-Elmer) was used in a hot-start protocol suggested by the manufacturer. The following conditions were used for amplification: denaturation at 94°C for 45 s, annealing at 50°C for 45 s, and elongation at 72°C for 45 s, with an additional 5 s being added for each cycle. A total of 25 cycles were performed and were followed by a final elongation step at 72°C for 15 min. The purity of the amplified product was determined by electrophoresis in a 1% agarose gel (FMC Bioproducts). DNA was stained with ethidium bromide and viewed under short-wavelength UV light.

TABLE 3. Comparison of cat strains with the type strain of *H. pylori*

Characteristic	Result[a] for:	
	Cat *H. pylori* strains	*H. pylori* NCTC 11637[T]
Oxidase	+ (6/6)	+
Catalase	+ (6/6)	+
Urease	+ (6/6)	+
Alkaline phosphatase	+ (4/4)	+
Hippurate hydrolysis	− (4/4)	−
Nitrate reduction	− (4/4)	−
H_2S production on triple sugar iron agar	− (4/4)	−
Indoxyl acetate hydrolysis	− (4/4)	−
Microaerophilic growth at:		
25°C	− (4/4)	−
37°C	+ (6/6)	+
42°C	− (4/4)	−
Aerobic growth at 37°C	− (4/4)	−
Growth on blood agar containing 3% NaCl	− (4/4)	−
Susceptibility to nalidixic acid	R (6/6)	R
Susceptibility to cephalothin	S (6/6)	S

[a] +, positive; −, negative; S, susceptible; R, resistant. Numbers in parentheses indicate ratio of number positive/number tested.

Purification of the PCR product. The amplified DNA was purified by precipitation with polyethylene glycol 8000 (22). After the removal of Ampliwax, a 0.6 volume of 20% polyethylene glycol 8000 (Sigma) in 2.5 M NaCl was added, and the mixture was incubated at 37°C for 10 min. The sample was centrifuged for 15 min at 15,000 × *g*, and the pellet was washed with 80% ethanol and pelleted as described above. The pellet was air dried, dissolved in 30 μl of distilled water, and used in cycle sequencing as described below.

Sequencing methods. The DNA sample from the PCR was directly sequenced by use of a cycle sequencing kit (TAQuence cycle sequencing kit; United States Biochemical Corp.). The manufacturer's protocol was followed. The five sequencing primers are shown in Table 1. Primers were end labeled with [^{33}P]ATP (NEN/Dupont) in accordance with the manufacturer's protocol. Approximately 100 ng of purified DNA from the PCR was used for sequencing. Reaction products were loaded onto 8% polyacrylamide–urea gels, electrophoresed, and detected by exposure of X-ray films for 24 h.

Sequence analysis. The program RNA, a program for data entry, editing, sequence alignment, secondary structure comparison, similarity matrix generation, and phylogenetic tree construction for 16S rRNA data, was used (33). rRNA sequences were read from the X-ray films, entered, and aligned as previously described (33).

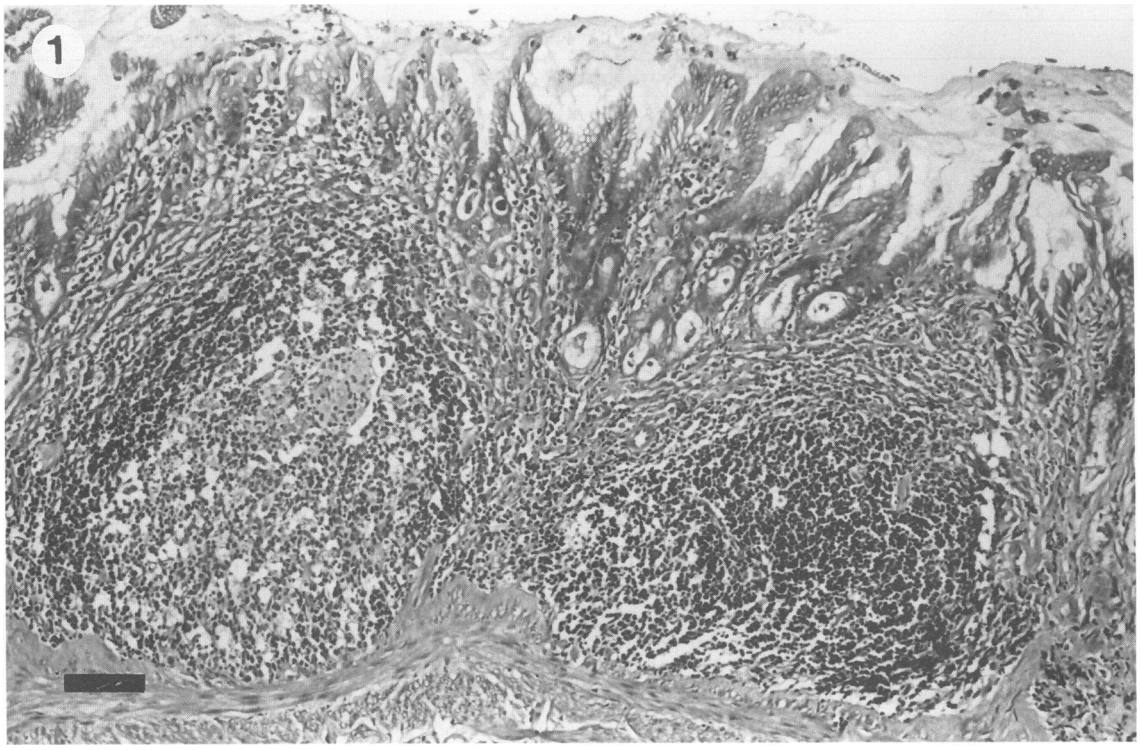
GenBank accession number. The sequence for cat *H. pylori* D01 has been deposited with GenBank under accession number U08906.

RESULTS

The detection of gastric spiral organisms with impression smears, urease tests, histologic evaluations, and culturing is summarized in Table 2.

Impression smears. Impression smears for the two cats tested from vendor A were negative for organisms. Smears for the two vendor C cats tested were positive for gram-negative, spiral-shaped organisms, which were 6 to 10 μm by 0.5 μm and had six to nine turns. For 13 of 15 vendor D cats tested, gram-negative, curved to spiral-shaped rods, which were 3 to 5 μm by 0.5 μm, were observed.

Rapid urease testing. Rapid urease testing of two vendor C cats resulted in samples from both the body and the antrum turning positive after 2 to 3 h. Body samples were positive for 13 of 16 vendor D cats, and antral samples yielded a positive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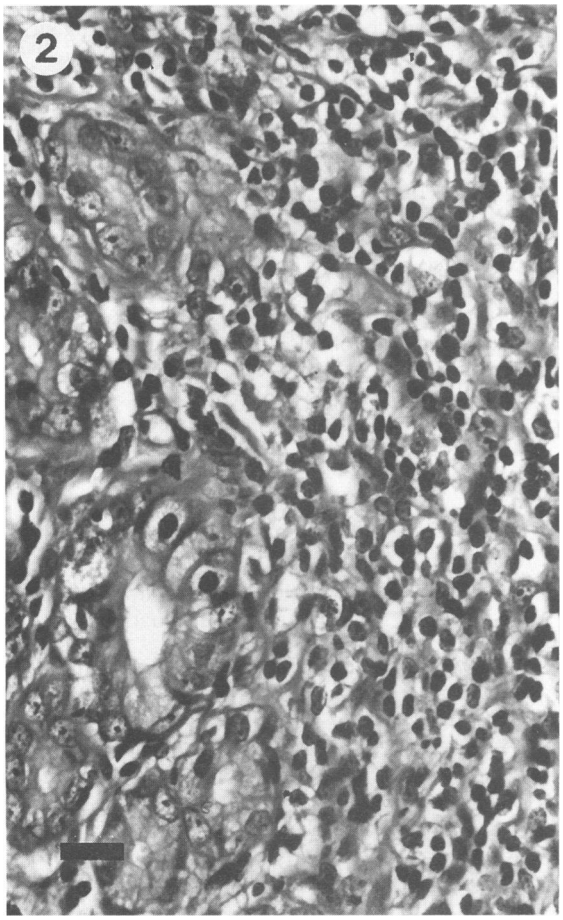
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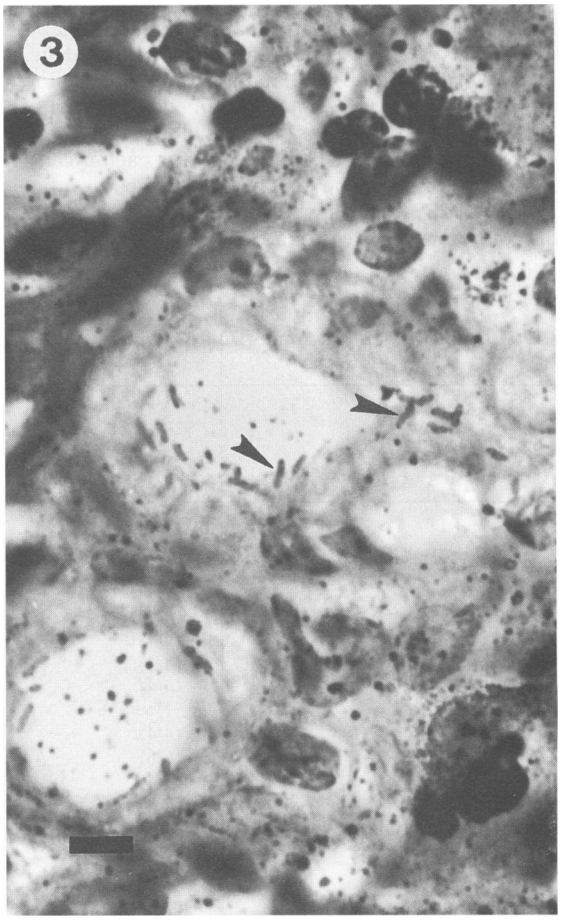
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TABLE 4. Histopathologic findings

Vendor	*H. pylori*	No. of cats	No. of cats with a gastritis score of >1[a] in:			Avg no. of follicles[b] in:		
			Cardia and fundus	Body	Antrum	Cardia and fundus	Body	Antrum
A	Negative	4	1	0	0	0	0	0
D	Positive	21	5	2	13	0.9[c]	0.7[c]	4.2[c]

[a] Gastritis scores: 0, normal; 1, mild inflammation; 2, moderate inflammation; 3, severe inflammation. See the text for details.
[b] Per ×20 microscopic field per animal.
[c] Significant difference between vendor A and D cats ($P < 0.001$).

result for 15 of the 16 cats. In most instances, antral samples were positive by 1 to 2 h, while biopsies from the body took 3 to 6 h to become positive.

Isolation of spiral organisms. Culturing of gastric tissue from one cat from vendor C yielded no growth. Pinpoint clear colonies were observed on both TVP and chocolate agar plates for cultures of gastric antral samples from eight cats from vendor D. Two of these bacterial cultures were subsequently lost because of failure of the microaerophilic environment before the organisms could be characterized. Similar colonies were cultured from gastric body samples from three of these cats. Although organisms could occasionally be seen on the culture plates by 3 days postinoculation, usually 5 days of incubation was necessary to visualize the colonies. For four of these animals, colonies were not grossly evident after 5 days; however, rubbing a sterile cotton applicator over the surface of the original plates and then restreaking the applicator on fresh culture medium produced visible bacterial colonies on the newly inoculated agar plates after 3 to 5 days of incubation.

Biochemical characterization of strains. The biochemical and culture characteristics of the vendor D cat strains are shown along with those of the type strain of *H. pylori* in Table 3.

Fatty acid analysis. Fatty acid analysis of *H. pylori* D01 revealed the following percentages (the number of carbon atoms in the fatty acid is to the left of the colon; the number of double bonds is to the right; w indicates the double bond position from the hydrocarbon end of the chain; and c and t indicate the *cis* and *trans* configurations of the hydrogen atoms, respectively) (40): 12:0 (0.71%), 13:1 at -12– -13 (0.42%), 14:0 (42.40%), 15:0 (0.54%), 16:0 (2.43%), 16:0 3OH (3.48%), 17:0 3OH (0.30%), 18:0 (9.14%), 18:1 w9c (0.40%), 19:0 (0.33%), 19:0 Cyclo w8c (22.58%), 19:1 w12t (0.52%), 20:0 (0.45%), 20:2 w6,9c (1.26%), and 20:3 w6,9,12c (5.74%). This analysis yielded a similarity index of 0.621 with the cataloged strain of *H. pylori*, with no other library strain within 0.100. According to the guidelines of the Microbial Identification System similarity index, any two strains with a similarity of 0.500 or higher and with a separation of 0.100 between the first and second choices are considered "very good" library comparisons (28). This library contains two *Helicobacter* species: *H. pylori* and *Helicobacter cinaedae*.

Histopathology. Histopathologic analysis of gastric tissue from vendor B and C cats, colonized with large gastric spiral organisms, revealed mild to moderate numbers of lymphocytes and plasma cells and occasional neutrophils in the lamina propria and superficial portion of the gastric mucosa. Multifocal lymphoid follicles originated in the subglandular region of the mucosa and extended towards the luminal surface. On sections from the vendor B cat and all three vendor C cats, large spiral-shaped organisms were seen in the gastric mucosa. These organisms were 6 to 10 μm by 0.5 μm and had five to nine helical turns. They were located in both the superficial mucus layer and the lumina of the gastric glands. In some cases, they appeared to be located intracellularly in the parietal cells. The organisms were consistently found in large numbers in the body of the stomach but were seen in the fundus and the antrum as well. One vendor A animal had moderate superficial gastritis present in the cardia and fundus, another had mild superficial gastritis in the body, and a third had mild gastritis in the antrum. All other sections from vendor A cats were normal. No gastric organisms or lymphoid follicles were observed in any of the four vendor A animals.

Five of 21 vendor D cats had moderate gastritis and 6 had mild gastritis in the cardia and fundus. Two of 21 vendor D cats had moderate gastritis and 9 had mild gastritis in the stomach body. Two, 11, and 6 vendor D animals had severe, moderate, and mild gastritis in the antrum, respectively. The average gastritis scores for the body, antrum, and stomach as a whole were significantly higher for vendor D cats than for vendor A cats ($P < 0.01$). Fifteen of 21 (71%) vendor D cats had moderate or severe gastritis in at least one region of the stomach, compared with 1 of 4 (25%) vendor A cats. Gastritis in *H. pylori*-infected cats (vendor D) consisted of mild to severe diffuse lymphoplasmacytic infiltrates with occasional neutrophils and eosinophils in the subglandular and glandular mucosae (Fig. 1–3).

Six of 21 vendor D cats had lymphoid follicles in the cardia and fundus, and 6 had follicles in the stomach body. Eighteen of 21 vendor D cats had lymphoid follicles in the antrum, with an average of 4.2 follicles per cat. These subglandular lymphoid follicles varied in size, with the larger follicles displacing glandular elements as the lymphoid follicles expanded. The number of lymphoid follicles in the cardia, and fundus, body, antrum, and stomach as a whole was significantly higher for vendor D cats than for vendor A cats ($P < 0.001$). The average number of follicles in all three regions of the stomach for vendor D cats was 5.8; that for vendor A cats was 0 ($P < 0.001$) (Table 4). For all 21 vendor D cats, histologic evaluation revealed the presence of comma- to spiral-shaped organisms, 3 to 5 μm by 0.5 μm, overlying the gastric mucosa. The organisms were located in close proximity to the mucosal epithelial cells, in the lumina of the gastric pits, and in the superficial mucus layer (Fig. 1–3). In the majority of the animals, the

FIG. 1. Cat antrum colonized with *H. pylori*. Glandular elements of mucosa effaced by extensive lymphoid hyperplasia, formation of lymphoid follicles in the mucosa and submucosa, and crypt dilation with intraluminal cellular debris can be seen. Hematoxylin and eosin stain. Bar, 72 μm.

FIG. 2. Cat antrum colonized with *H. pylori*. Extensive lymphoplasmacytic infiltration displacing glands in the lamina propria can be seen. Hematoxylin and eosin stain. Bar, 45 μm.

FIG. 3. Cat antrum with *H. pylori* (arrowheads) on the surface of the crypt epithelium. Warthin-Starry stain. Bar, 8 μm.

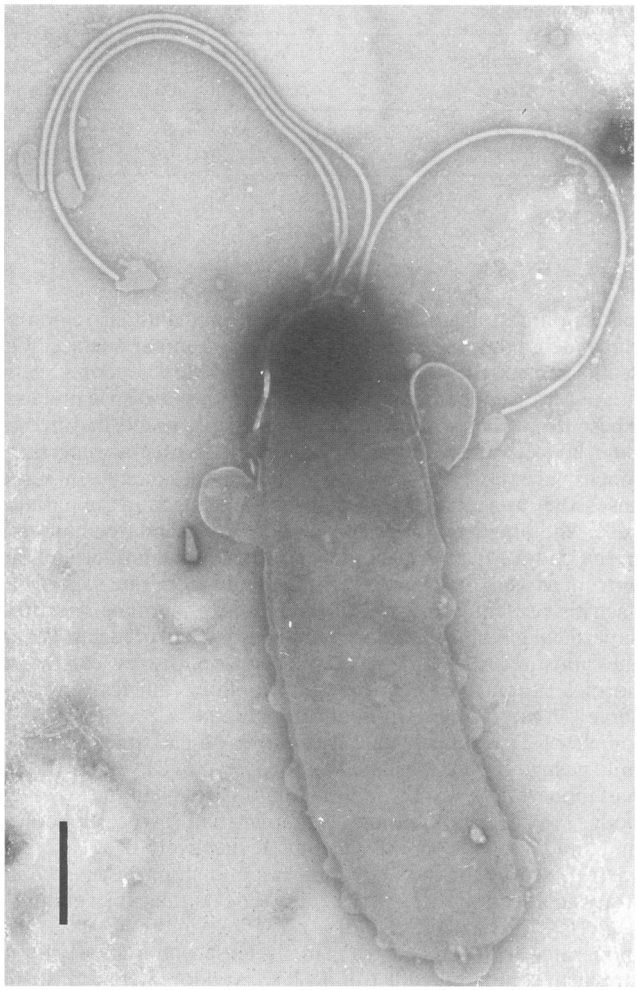

FIG. 4. Negatively stained cell of *H. pylori* D01. Note multiple sheathed flagella originating from one end of the cell. Remnants of a flagellum originating from the other end can be seen. Bar, 0.5 μm.

bacteria were seen in large numbers in the fundus, body, and antrum. Twenty of the 21 cats had a 3+ quantity of organisms in at least one of the three areas of the stomach examined. The remaining cat had only a 1+ quantity of organisms in all three stomach areas.

Ultrastructure. The ultrastructural characteristics of the cat strains were similar to those described for strains of *H. pylori*. Cells varied in shape from curved to spiral and measured 2 to 6 μm in length by 0.5 μm in width. Four to six sheathed flagella originated from one end of the organism (Fig. 4). Some cells possessed a single polar sheathed flagellum at the other end.

16S rRNA sequence. A single band of approximately 1,500 bp was seen by agarose gel electrophoresis following PCR amplification of the 16S rRNA cistrons of cat isolate D01. The sequence for this amplicon was obtained by cycle sequencing and is available from GenBank under accession number U08906. The sequence (1,475 bases) was compared against our data base for strains representing more than 24 *Helicobacter* species and 300 species of other bacteria. The sequence of cat isolate D01 was 99.7% similar to that of the type strain of *H. pylori*. The cat sequence differed by 5 bases, typical of the minor variation seen in other sequenced *H. pylori* strains (5). Thus, on the basis of 16S rRNA sequence analysis, cat strain D01 is clearly a strain of *H. pylori*.

DISCUSSION

The goal of this research was to identify the types of gastric spiral organisms present in cats from commercial vendors. The culturing and identification of *H. pylori* from vendor D cats were unexpected but demonstrate the utility of molecular techniques (such as 16S rRNA sequencing) for definitive identification. The presumptive identification of *H. pylori* in vendor D cats was based on morphologic characteristics and a biochemical evaluation of isolates from the six cats examined. The 16S rRNA sequence analysis and fatty acid analysis performed on strain D01 confirmed its identity as *H. pylori*. All 15 remaining vendor D animals for which culturing was not attempted or was not successful had organisms comparable to *H. pylori*, as determined visually on histologic examination. *H. pylori* appeared to be most prevalent in the antrum but in many animals was also seen in large numbers in the fundus and body. The large spiral organisms seen in all four cats from vendors B and C appeared to be either *H. felis* or the large "gastrospirillum" commonly observed in cats. It is not surprising that we were unable to isolate organisms from these cats, as *H. felis* can be difficult to culture and "gastrospirillum" organisms are thus far uncultivable. We are currently using PCR amplification of 16S rRNA cistrons and sequencing to attempt to identify *Helicobacter* species present in fixed tissues from cats from vendors B and C.

All cats from each vendor had gastric organisms that were morphologically similar, implying that gastric helicobacters are efficient colonizers in cats sharing the same commercial facilities. The isolation of *H. pylori* from the cats which were sampled soon after arrival at our vivarium strongly supports the premise that these cats were already infected with the organism prior to our receipt of them. Also, our subsequent individual housing of the animals and the fact that no gastric manipulations were performed on them further mitigate against the acquisition by the cats of *H. pylori* while they were housed at our animal research facility. The identification of *H. pylori* in cats housed for several months in our research facility supports our hypothesis that cats, like humans, can be persistently colonized with this organism.

Appropriate animal models of human *H. pylori* disease are needed for further study of the organism. Until now, the only other naturally occurring hosts found for *H. pylori* had been several species of nonhuman primates (2, 3, 30). These animals consistently develop chronic gastritis when naturally infected with *H. pylori* (2, 30). However, many of these nonhuman primates also harbor other gastric spiral organisms, a complicating factor in their use as models (3, 36). Gnotobiotic dogs and gnotobiotic pigs develop chronic gastritis when experimentally infected with *H. pylori* (21, 35). A preliminary report indicates that nude mice also develop chronic gastritis when experimentally infected with *H. pylori* (18). The discovery of *H. pylori* in cats suggests that this species may be useful as a model of human *H. pylori* disease. The large numbers of *H. pylori* organisms present in the stomachs of the cats in this report allowed easy histologic detection and in vitro culturing. One disadvantage of the use of the cat as a model for *H. pylori* studies is gastric colonization with the other spiral organisms frequently observed in this species. In contrast to the active chronic gastritis, with appreciable neutrophilic cell infiltrates, seen in many humans with *H. pylori* disease, the *H. pylori* chronic gastritis seen in cats, which was severe in some cats, consisted mostly of lymphoplasmacytic cell infiltrates. The

presence of *H. pylori* in gastric tissue strongly supports the causal role of this bacterium in the development of gastritis. The multifocal lymphoplasmacytic infiltrate which often forms lymphoid follicles in *H. pylori*-infected cats has been described elsewhere for natural or experimental gastric helicobacter infections in cats, dogs, and ferrets (8, 15, 16, 26, 31, 35). It will be of interest to study cats which have been colonized with *H. pylori* for a longer duration and cats which have been subjected to different environmental conditions or dietary changes to ascertain if differences in the gastritis profile occur with manipulation of these variables.

The mechanism and patterns of transmission of *H. pylori* infection are poorly understood. Direct person-to-person spread of *H. pylori* is suspected, on the basis of the increased prevalence of infection in certain families and institutions, such as nursing homes (4, 19). Both oral-oral transmission and fecal-oral transmission have been postulated as a means of spread of *H. pylori* from person to person (25, 39). The isolation of *H. pylori* from human feces supports the role of fecal-oral transmission of the organism (39). Infection from a common endogenous source also remains a possibility, but an environmental reservoir of the organism has not been positively identified. Contaminated water and vegetables sprayed with contaminated water have been incriminated in developing countries (17, 20). The isolation of *H. pylori* from domestic cats implies that reservoir hosts may play a role in transmission as well.

Because cats are popular pets, significant cat-human contact occurs, and this contact could potentiate the transmission of *H. pylori*. Although we have not documented passage by infected cats of viable *H. pylori* organisms in feces, another carnivore, the ferret, does shed viable gastric *Helicobacter mustelae* organisms in feces (12). The presence of *H. pylori* in cat feces is a likely source of transmission of the organism, since humans are consistently exposed to cat feces when cleaning litter boxes. Certainly, cats are well-established reservoir hosts for zoonotic infections with other fecally transmitted bacteria, such as *Campylobacter jejuni* and *Salmonella* spp. (6). Furthermore, since many cats vomit occasionally and cats are continually grooming, the oral-oral route of transmission to humans is also a possibility.

Previous speculation about the zoonotic potential of gastric spiral organisms from domestic felines has centered on *H. felis* and the large "gastrospirillum" commonly observed in cats (23, 27, 31). Our report raises the possibility that *H. pylori* infection may be a zoonotic disease, with transmission occurring from cats to humans. Studies are ongoing to define the prevalence of *H. pylori* infection in pet and laboratory-maintained cats, to explore the possible routes of transmission of the organism between cats and humans and, importantly, to ascertain whether *H. pylori* is indeed a zoonotic pathogen. Molecular identification of additional cultivable and uncultivable gastric spiral organisms in cats is in progress.

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